REMARKS

The Office Action mailed June 17, 2004 has been carefully reviewed and the foregoing amendments are made in response thereto. In view of the amendments and the following remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Objection to the Claims

Claim 39 was objected to because of a typographical error resulting in the inclusion of an "a" in the array providing step. Applicants have amended the claim to remove the "a".

Rejection under 35 USC § 112, second paragraph

Applicants have amended claim 57 to clarify that the second nucleic acid sample comprises the DNA duplexes isolated after digestion of the duplexes bound to the magnetic beads.

Rejection under 35 USC § 112, first paragraph

Claim 47 has been amended to clarify that only the fragmentation, adaptor ligation and amplification steps are performed in a single reaction vessel and not array hybridization.

Rejections under 35 USC § 103(a)

Claims 39-53 have been rejected over McCasky Feazel *et al.* (U.S. Patent No. 6,100,030) in view of DeRisis et al. (Science 278:680-686, 1997) and Moyer et al. (Applied and Environmental Microbiology 62:2501-2507, 1996).

Claim 39, from which claims 40-53 depend, has been amended to more clearly describe the relationship between the method of complexity reduction and the design of the array used to analyze the second nucleic acid sample. The complexity of the sample is reduced in a reproducible way using a selected fragmentation method, adaptors are ligated to the fragments and the fragments are subjected to a selected amplification

method. The combination of the selected fragmentation method and selected amplification method results in a reproducible set of amplified fragments. A computer system is used to predict the size and sequence of fragments that will result from the selected fragmentation method, predict which fragments will be amplified by the selected amplification method and then to identify polymorphisms within the fragments that will be amplified. An array is designed to interrogate the genotype of at least some of those polymorphisms and the amplified sample is hybridized to the array. The complexity of the sample is reduced in a reproducible and predictable manner by a pre-selected method of fragmentation and amplification and the array is designed to interrogate polymorphisms in samples subjected to that pre-selected complexity reduction method.

McCasky Feazel et al. does not disclose a method of reducing the complexity of a sample and hybridizing the reduced complexity sample to an array designed to interrogate polymorphisms predicted by a computer to be present in the reduced complexity sample. Moyer et al. fails to remedy the deficiencies of McCasky Feazel et al. Moyer et al. discloses a method of using a computer simulation to predict the size of fragments resulting when a specific nucleic acid fragment is digested with a restriction enzyme. Differences in fragment size are identified between different bacteria but the sequences of the fragments are not analyzed to identify polymorphisms within the fragments. Moyer et al. also fails to teach the use of a computer system to identify fragments that will be amplified by a selected amplification method or to identify polymorphisms within the amplified fragments. Reconsideration and withdrawal of the rejection of claims 39-53 is respectfully requested.

CONCLUSION

For the foregoing reasons, Applicants believe all the pending claims are now in condition for allowance and should be passed to issue. Applicants believe that no extension of time is required for submission of this paper. However, if an extension is required, Applicants petition for any necessary extension of time and authorize the Commissioner to deduct any required fees from the undersigned's Deposit Account No. 01-0431. Please deduct any additional fees from, or credit any overpayment to the above-noted Deposit Account. If the Examiner feels that a telephone conference would in any way expedite the prosecution of the application, please do not hesitate to call the undersigned at (408) 731-5768.

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Respectfully submitted,

Sandra E. Wells
Reg. No. 52,349

Customer No. 22886
Legal Department
Affymetrix, Inc.
3380 Central Expressway
Santa Clara, CA 95051
Tel: 408/731-5768
Fax: 408/731-5392